

**Hart, Edward**

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**Fr m:** O'Bryen, Barbara  
**Sent:** Monday, January 05, 2004 9:56 AM  
**T :** Hart, Edward  
**Cc:** Rao, Manjunath N.  
**Subject:** RE: Sequence search request for 10/037,270

Edward,  
According to Access (107718), you completed this search on 11-12-03. Apparently the results never made it to the examiner. Please provide him with another copy.  
Thanks,  
Barb

-----Original Message-----

**From:** Rao, Manjunath N.  
**Sent:** Monday, January 05, 2004 9:44 AM  
**To:** STIC-Biotech/ChemLib  
**Subject:** FW: Sequence search request for 10/037,270

This search request was e-mailed on 11-5-03. I have so far not received the search results. Please let me know the status of the search request.

Thanks  
Manjunath

-----Original Message-----

**From:** Rao, Manjunath N.  
**Sent:** Wednesday, November 05, 2003 1:09 PM  
**To:** STIC-Biotech/ChemLib  
**Subject:** Sequence search request for 10/037,270

**From:** Manjunath N. Rao  
Art Unit 1652, Room 10A11  
Mail Box in Room 10D 01  
Phone: 306-5681

**Date:** 11-5-03

Please search the following as soon as possible for application with serial number

**10/037,270**

1. SEQ ID NO: 482 against all commercial nucleic acid databases, commercial amino acid databases, issued patents/published applications database and pending application database. Please provide a print of all results

If you have any questions please call me at the above phone number.

Thanks

**Manjunath N. Ra , Ph.D.**  
**Biotechnology Patent Examiner**  
**Art Unit 1652, Room 10A11**  
**Mail Box in 10D01**  
**Crystal Mall 1, USPTO.**

=> d his

(FILE 'HOME' ENTERED AT 10:03:23 ON 05 JAN 2004)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,  
BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,  
CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS,  
DDFB, DDFU, DGENE, DRUGB, DRUGMONOG2, ...' ENTERED AT 10:03:30 ON 05 JAN  
2004

SEA TRYPSINOGEN

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3 FILE ADISCTI  
72 FILE AGRICOLA  
74 FILE ANABSTR  
44 FILE AQUASCI  
10 FILE BIOBUSINESS  
11 FILE BIOCOMMERCE  
1814 FILE BIOSIS  
59 FILE BIOTECHABS  
59 FILE BIOTECHDS  
410 FILE BIOTECHNO  
165 FILE CABA  
166 FILE CANCERLIT  
1984 FILE CAPLUS  
11 FILE CEABA-VTB  
1 FILE CEN  
5 FILE CIN  
31 FILE CONFSCI  
58 FILE DISSABS  
94 FILE DDFB  
72 FILE DDFU  
630 FILE DGENE  
94 FILE DRUGB  
85 FILE DRUGU  
8 FILE EMBAL  
1358 FILE EMBASE  
401 FILE ESBIODASE  
16 FILE FEDRIP  
7 FILE FROSTI  
14 FILE FSTA  
5724 FILE GENBANK  
49 FILE IFIPAT  
168 FILE JICST-EPLUS  
2 FILE KOSMET  
180 FILE LIFESCI  
1749 FILE MEDLINE  
2 FILE NIOSHTIC  
11 FILE NTIS  
18 FILE OCEAN  
542 FILE PASCAL  
15 FILE PHIN  
13 FILE PROMT  
1 FILE RDISCLOSURE  
1326 FILE SCISEARCH  
723 FILE TOXCENTER  
678 FILE USPATFULL  
12 FILE USPAT2  
4 FILE VETU  
48 FILE WPIDS  
48 FILE WPINDEX

QUE TRYPSINOGEN  
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FILE 'CAPLUS, BIOSIS, MEDLINE, EMBASE, SCISEARCH, TOXCENTER, USPATFULL,  
PASCAL, BIOTECHNO, ESBIODASE, LIFESCI, JICST-EPLUS, CANCERLIT, CABA'  
ENTERED AT 10:04:43 ON 05 JAN 2004

L2 3267 S L1 AND (ISOLAT? OR PURIF? OR CHARACT?)  
L3 1612 DUP REM L2 (1655 DUPLICATES REMOVED)  
L4 866 S L3 AND PD=<1999  
L5 46 S L4 AND CHICK?  
L6 335 S L4 AND HUMAN

=> log Y

=> d 16 ibib ab 330-335

L6 ANSWER 330 OF 335 USPATFULL on STN  
ACCESSION NUMBER: 78:4744 USPATFULL  
TITLE: Substrate for the quantitative determination of  
proteolytic enzymes  
INVENTOR(S): Svendsen, Lars Gundro, Reinach, Switzerland  
PATENT ASSIGNEE(S): Pentapharm A.G., Basel, Switzerland (non-U.S.  
corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4070245		19780124	<--
APPLICATION INFO.:	US 1976-697550		19760618	(5)

	NUMBER	DATE
PRIORITY INFORMATION:	CH 1975-8224	19750623
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Naff, David M.	
LEGAL REPRESENTATIVE:	Pennie & Edmonds	
NUMBER OF CLAIMS:	18	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 3 Drawing Page(s)	
LINE COUNT:	1328	

AB A substrate for the quantitative determination of enzymes in  
human and mammal body fluids as well as in animal cell extracts  
and glandular venoms of cold-blooded animals, which has the structure

R.sup.1 -- Gly -- Pro -- X -- NH -- R.sup.2

wherein R.sup.1 represents hydrogen or a blocking acyl or sulfonyl  
group, R.sup.2 represents an aromatic hydrocarbon group which may carry  
substituents and X represents arginyl or lysyl, --NH--R.sup.2 being a  
chromogenic or fluorescent group capable of yielding a split product  
NH.sub.2 --R.sup.2 the quantity of which can be measured by photometric,  
spectrophotometric or fluorescence-photometric methods.

L6 ANSWER 331 OF 335 USPATFULL on STN  
ACCESSION NUMBER: 77:40368 USPATFULL  
TITLE: Fibrinolytic substances  
INVENTOR(S): King, John Burnham, Sandown Lodge, Glebe Road,  
Rondebosch, Cape, South Africa

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4039658		19770802	<--
APPLICATION INFO.:	US 1975-628006		19751103	(5)
RELATED APPLN. INFO.:	Division of Ser. No. US 1973-347254, filed on 2 Apr. 1973, now abandoned			

	NUMBER	DATE
PRIORITY INFORMATION:	ZA 1972-2311	19720405
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Shapiro, Lionel M.	
LEGAL REPRESENTATIVE:	Behr & Woodbridge	
NUMBER OF CLAIMS:	13	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	406	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A new fibrinolytic enzymatic product having also anticoagulant properties is recovered from bile. It can be further purified to yield several fractions, all having similar activities, their molecular weights varying between about 5,000 and 50,000. The product or its fibrinolytically active derivatives are used to dissolve fibrin and inhibit blood coagulation in vivo or in vitro.

L6 ANSWER 332 OF 335 USPATFULL on STN  
 ACCESSION NUMBER: 77:21167 USPATFULL  
 TITLE: Agarose containing affinity matrix materials  
 INVENTOR(S): Nishikawa, A. Hirotooshi, Webster, NY, United States  
 Hixson, Jr., Harry F., Webster, NY, United States  
 PATENT ASSIGNEE(S): Xerox Corporation, Stamford, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4020268		19770426 <--
APPLICATION INFO.:	US 1974-526028		19741121 (5)
RELATED APPLN. INFO.:	Division of Ser. No. US 1972-306241, filed on 13 Nov 1972, now abandoned which is a division of Ser. No. US 1971-141778, filed on 12 May 1971, now patented, Pat. No. US 3746622		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Brown, Johnnie R.		
NUMBER OF CLAIMS:	1		
EXEMPLARY CLAIM:	1		
LINE COUNT:	374		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel affinity matrix material for trypsin and trypsin-like enzymes is disclosed. Methods employing this material to isolate and/or purify crude extracts containing trypsin and trypsin-like enzymes and to store the purified enzymes obtained are also disclosed.

L6 ANSWER 333 OF 335 USPATFULL on STN  
 ACCESSION NUMBER: 76:26340 USPATFULL  
 TITLE: Preparing pancreatin  
 INVENTOR(S): Lewis, deceased, Sheldon H., late of Chicago Heights, IL, United States BY Barbara Lewis, administratrix  
 PATENT ASSIGNEE(S): Wilson Pharmaceutical & Chemical Corporation, Chicago, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3956483		19760511 <--
APPLICATION INFO.:	US 1971-144230		19710517 (5)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1968-770443, filed on 24 Oct 1968, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Drezin, Norman A.		
NUMBER OF CLAIMS:	4		
EXEMPLARY CLAIM:	1		
LINE COUNT:	350		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention deals with compositions having utility as digestive aids. Such compositions can be produced in a dry powder form, with amylolytic and lipolytic activity in addition to the proteolytic activity normally present and with harmful bacteria eliminated therefrom by treating comminuted pancreas with aqueous medium containing calcium sulfate or calcium acetate, adding a proteolytic enzyme activator and after a

period required for enzyme activation, dehydrating the mixture at temperatures which will inactivate pathogenic bacteria.

L6 ANSWER 334 OF 335 USPATFULL on STN  
ACCESSION NUMBER: 75:35715 USPATFULL  
TITLE: N-acylated peptides of amino aromatic sulfonic acids and their derivatives  
INVENTOR(S): De Benneville, Peter L., Philadelphia, PA, United States  
PATENT ASSIGNEE(S): Rohm and Haas Company, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3893992		19750708 <--
APPLICATION INFO.:	US 1973-424020		19731212 (5)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1970-91176, filed on 19 Nov 1970, now patented, Pat. No. US 3801562, issued on 2 Apr 1974		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Gotts, Lewis		
ASSISTANT EXAMINER:	Suyat, Reginald J.		
NUMBER OF CLAIMS:	11		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1111		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Polypeptides which are useful for evaluating pancreatic enzyme sufficiently in animal organisms have the formula

RCO--A.sub.n --NHR'CO--B.sub.m --NHZ

wherein

R is a hydrogen atom; a phenyl group; a phenyl group substituted with one or more halogen atoms, (C.sub.1 --C.sub.4)alkyl groups, hydroxy groups, (C.sub.1 --C.sub.4)alkoxy groups, (C.sub.1 --C.sub.4)alkoxy carbonyl groups, or similar substituents which will not interfere with the test efficacy of the polypeptide; a (C.sub.1 --C.sub.12)alkyl group, preferably a (C.sub.1 --C.sub.6)alkyl group; a (C.sub.1 --C.sub.12)alkyl group substituted by one or more halogen atoms, (C.sub.1 --C.sub.4)alkoxy groups, hydroxy groups, acyloxy groups, preferably (C.sub.1 --C.sub.4)alkanoyloxy or benzoyloxy, polyalkoxyalkyl groups, phenyl groups, or similar substituents which will not interfere with the test efficacy of the polypeptide; a (C.sub.1 --C.sub.12)alkoxy group, preferably a (C.sub.1 --C.sub.6)alkoxy group; an aryloxy group having up to 10 carbon atoms; or a divalent alkylene group having up to 6 carbon atoms, in which case the formula would be written as

R(--CO A.sub.n --NHR'CO--B.sub.m --NHZ).sub.2

or, when the blocking group is derived from oxalic acid, as

(CO--A.sub.n --NHR'CO--B.sub.m --NHZ).sub.2

Nhr'co is the amino acid linkage derived from L-phenylalanine, L-tyrosine, L-leucine, L-methionine, L-tryptophan, L-arginine, or L-lysine;

Z is a group of the formula ##SPC1##

Wherein

R" is a hydroxy group, a (C.sub.1 --C.sub.4)alkoxy group, a (C.sub.1

--C.sub.4)alkoxyalkoxy group, a (C.sub.1 --C.sub.8)aminoalkoxy group, an amino group, a (C.sub.1 --C.sub.4)monoalkylamino group, a (C.sub.1 --C.sub.4)dialkylamino group, a group of the formula --NHCH.sub.2 COR", or a salt, such as the sodium, potassium, or ammonium salt, of the group in which R" is a hydroxy group;

Y is a group of the formula --CO-- or --SO.sub.2 --;

X is a hydroxy group, a (C.sub.1 --C.sub.4)alkyl group, a halogen atom, a (C.sub.1 --C.sub.4)alkoxy group, or a similar substituent which will not interfere with the test efficacy of the polypeptide; and

n' is 0, 1, or 2;

A and B are the residues of low molecular weight amino acids, such as glycyl, alanyl, glycyglycyl, and the like, and

n and m are 0, 1, or 2.

L6 ANSWER 335 OF 335 LIFESCI COPYRIGHT 2004 CSA on STN

ACCESSION NUMBER: 88:60053 LIFESCI

TITLE: Possible lysosomal activation of pancreatic zymogens.  
Activation of both **human trypsinogens**  
by cathepsin B and spontaneous acid activation of  
**human trypsinogen 1**.

AUTHOR: Figarella, C.; Miszczuk-Jamska, B.; Barrett, A.J.

CORPORATE SOURCE: Groupe Rech. Glandes Exocrines, 27 Blvd. Lei Roure, 13273  
Marseille Cedex 09, France

SOURCE: BIOL. CHEM. HOPPE-SEYLER., (1988) vol. 369, no.  
suppl., pp. 293-298.  
Meeting Info.: Protein Inhibitors and Biological Control.  
Ljubljana/Brno (Yugoslavia). 4-7 Jul 1987.

DOCUMENT TYPE: Journal

TREATMENT CODE: Conference

FILE SEGMENT: L

LANGUAGE: English

SUMMARY LANGUAGE: English

AB **Human trypsinogens 1 and 2** were activated at the same rate by pure **human cathepsin B** at pH 3.8. **Human trypsinogen 1** was also spontaneously activated during incubation at acidic pH, activation being most rapid at pH 5.0. In contrast, **trypsinogen 2** showed little or no activation under these conditions. The presence of calcium salts (20 mM) delayed the onset of activation under all conditions tested.

=> d 16 ibib ab 319-329

L6 ANSWER 319 OF 335 USPATFULL on STN

ACCESSION NUMBER: 85:29854 USPATFULL

TITLE: **Purification and activity assurance of precipitated heterologous proteins**

INVENTOR(S): Olson, Kenneth C., Burlingame, CA, United States

PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4518526		19850521.	<--
APPLICATION INFO.:	US 1984-615682		19840601	(6)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1982-452356, filed on 22 Dec 1982			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			



PRIMARY EXAMINER: Schain, Howard E.  
NUMBER OF CLAIMS: 11  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 6 Drawing Page(s)  
LINE COUNT: 1607

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for isolating and purifying a precipitated heterologous protein from a host cell culture, including treating the host cell culture with a buffered solution of ionic strength suitable to solubilize most of the host protein but in which refractile heterologous protein is substantially insoluble, and disrupting the cells to form a supernatant and an insoluble fraction; treating the insoluble fraction with a strongly denaturing solution to solubilize the refractile heterologous protein; and recovering renatured heterologous protein.

L6 ANSWER 320 OF 335 USPATFULL on STN

ACCESSION NUMBER: 85:25427 USPATFULL

TITLE: Amidine compound, process for producing same and anti-complement agent comprising same

INVENTOR(S): Fujii, Setsuro, Toyonaka, Japan  
Yaegashi, Takashi, Funabashi, Japan  
Nakayama, Toyoo, Funabashi, Japan  
Sakurai, Yojiro, Kamakura, Japan  
Nunomura, Shigeki, Chiba, Japan  
Okutome, Toshiyuki, Tokyo, Japan  
PATENT ASSIGNEE(S): Torii & Co. Ltd., Tokyo, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4514416		19850430	<--
APPLICATION INFO.:	US 1984-611937		19840521	(6)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1982-350963, filed on 22 Feb 1982, now abandoned			

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1981-27974	19810227
	JP 1981-140650	19810907
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Shippen, Michael L.	
LEGAL REPRESENTATIVE:	Beveridge, DeGrandi & Weilacher	
NUMBER OF CLAIMS:	7	
EXEMPLARY CLAIM:	1	
LINE COUNT:	2134	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Amidino compounds represented by the formula (I) ##STR1## and pharmaceutically acceptable acid addition salts thereof are novel compounds and are useful as powerful antitrypsine, antiplasmin, antikallikrein and anti-thrombin agents. Having strong anti-Cl (Clr, Cls) activities and an anticomplement activity, they are also useful as anticomplement agents. These amidino compounds are prepared by usual esterification of carboxylic acid compounds represented by the formula (II)

R.sub.1 --COOH

(II)

with amidinophenol compound (III) and, if necessary, can be transformed into pharmaceutically acceptable acid addition salts thereof. ##STR2##

L6 ANSWER 321 OF 335 USPATFULL on STN

ACCESSION NUMBER: 85:23828 USPATFULL

TITLE: Purification and activity assurance of precipitated heterologous proteins

INVENTOR(S): Jones, Andrew J. S., San Mateo, CA, United States  
Olson, Kenneth C., Burlingame, CA, United States  
Shire, Steven J., San Mateo, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4512922		19850423 <--
APPLICATION INFO.:	US 1984-615679		19840601 (6)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1982-452253, filed on 22 Dec 1982, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Schain, Howard E.		
NUMBER OF CLAIMS:	9		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	1590		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for maintaining refractile proteins in solubilized form by replacing the strongly denaturing solution with a weakly denaturing solution.

L6 ANSWER 322 OF 335 USPATFULL on STN  
ACCESSION NUMBER: 85:22306 USPATFULL  
TITLE: Purification and activity assurance of precipitated heterologous proteins  
INVENTOR(S): Olson, Kenneth C., Burlingame, CA, United States  
Pai, Rong-Chang, Foster City, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4511503		19850416 <--
APPLICATION INFO.:	US 1984-615680		19840601 (6)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1982-452252, filed on 22 Dec 1982		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Schain, Howard E.		
NUMBER OF CLAIMS:	2		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	1528		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for dissolving refractile proteins from their insoluble form by using a strongly denaturing solution.

L6 ANSWER 323 OF 335 USPATFULL on STN  
ACCESSION NUMBER: 85:22305 USPATFULL  
TITLE: Purification and activity assurance of precipitated heterologous proteins  
INVENTOR(S): Builder, Stuart E., Belmont, CA, United States  
Ogez, John R., San Mateo, CA, United States  
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4511502		19850416 <--
APPLICATION INFO.:	US 1984-615676		19840601 (6)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1982-452355, filed on 22		

Dec 1982  
DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Schain, Howard E.  
NUMBER OF CLAIMS: 12  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 6 Drawing Page(s)  
LINE COUNT: 1607

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for purifying heterologous proteins from higher molecular weight components, including dissolving the heterologous protein in a strong denaturing solution and removing the higher molecular weight components using a molecular sieve or high speed centrifugation.

L6 ANSWER 324 OF 335 USPATFULL on STN  
ACCESSION NUMBER: 84:62325 USPATFULL  
TITLE: Aromatic polysulfone type resin hollow fiber membrane and process for producing the same  
INVENTOR(S): Nohmi, Takashi, Fuji, Japan  
PATENT ASSIGNEE(S): Asahi Kasei Kogyo Kabushiki Kaisha, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4481260		19841106	<--
APPLICATION INFO.:	US 1983-461992		19830128	(6)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1982-12864	19820129

DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Kendell, Lorraine T.  
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner  
NUMBER OF CLAIMS: 2  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 15 Drawing Figure(s); 15 Drawing Page(s)  
LINE COUNT: 1560

AB An aromatic polysulfone type resin hollow fiber membrane having a thickness of less than 100 .mu.m and a three-layer structure of inner and outer surface skin layers and a void layer disposed therebetween and connected thereto. The hollow fiber membrane of the kind has an improved burst strength, while exhibiting an extremely excellent water permeability. Such a hollow fiber membrane can be produced by a process which comprises extruding a spinning solution of an aromatic polysulfone type resin in an organic polar solvent for said resin, said solution containing a glycol and having a resin concentration of from 10 to 35% by weight, from an annular spinning nozzle of which the orifice width is 10 to 110 .mu.m while simultaneously injecting an internal coagulating liquid into the annular spinning nozzle at an inside bore thereof, thereby to obtain an extrudate in the form of a hollow fiber, and introducing said extrudate into an external coagulating liquid.

L6 ANSWER 325 OF 335 USPATFULL on STN  
ACCESSION NUMBER: 82:53250 USPATFULL  
TITLE: Method of incorporating water-soluble heat-sensitive therapeutic agents in albumin microspheres  
INVENTOR(S): Senyei, Andrew E., Chicago, IL, United States  
Widder, Kenneth J., Chicago, IL, United States  
PATENT ASSIGNEE(S): Northwestern University, Evanston, IL, United States (U.S. corporation)

NUMBER	KIND	DATE
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PATENT INFORMATION: US 4357259 19821102 <--  
 APPLICATION INFO.: US 1977-859842 19771212 (5)  
 RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1977-820812, filed  
 on 1 Aug 1977, now abandoned  
 DOCUMENT TYPE: Utility  
 FILE SEGMENT: Granted  
 PRIMARY EXAMINER: Lovering, Richard D.  
 NUMBER OF CLAIMS: 4  
 EXEMPLARY CLAIM: 1  
 LINE COUNT: 429  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is provided for incorporating water-soluble therapeutic agents  
 in albumin microspheres. This method is particularly advantageous where  
 the therapeutic agent is heat-sensitive. All steps of the method can be  
 carried out at relatively low temperatures, such as ambient room  
 temperature. The method may be applied to the preparation of  
 intravascularly-administrable, magnetically-responsive microspheres.

L6 ANSWER 326 OF 335 USPATFULL on STN  
 ACCESSION NUMBER: 81:38464 USPATFULL  
 TITLE: Method for the quantitative determination of  
 plasminogen activators  
 INVENTOR(S): Svendsen, Lars G., Reinach BL, Switzerland  
 PATENT ASSIGNEE(S): Pentapharm AG, Basel, Switzerland (non-U.S.  
 corporation)

NUMBER	KIND	DATE
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PATENT INFORMATION: US 4278762 19810714 <--  
 APPLICATION INFO.: US 1979-74551 19790911 (6)  
 RELATED APPLN. INFO.: Division of Ser. No. US 1977-798426, filed on 19 May  
 1977, now patented, Pat. No. US 4190574, issued on 26  
 Feb 1980

NUMBER	DATE
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PRIORITY INFORMATION: CH 1976-6816 19760528  
 DOCUMENT TYPE: Utility  
 FILE SEGMENT: Granted  
 PRIMARY EXAMINER: Castel, Benoit  
 LEGAL REPRESENTATIVE: Pennie & Edmonds  
 NUMBER OF CLAIMS: 5  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)  
 LINE COUNT: 1361

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a method for the quantitative  
 determination of enzymes in human and mammal body fluids and  
 tissue extracts, using a substrate which has the structure

R.sup.1 --X--Y--Z--NH--R.sup.2

wherein X represents a group having the formula ##STR1## in which  
 R.sup.3 is a straight or branched alkyl radical having 1 to 7 carbon  
 atoms or a cyclohexyl or cyclohexylmethyl radical, Y represents a seryl  
 group or a group having the formula --NH--(CH.sub.2).sub.n --CO-- in  
 which n is an integer from 1 to 7, Z represents an arginyl or lysyl  
 group, R.sup.1 represents hydrogen or an acyl or sulfonyl group and  
 R.sup.2 represents an aromatic hydrocarbon radical which optionally may  
 carry substituents. The method includes measuring by photometric,  
 spectrophotometric or fluorescence-photometric methods the quantity of  
 the split product NH.sub.2 R.sup.2 formed by the hydrolytic action of  
 the biologically active factors on the substrate.

L6 ANSWER 327 OF 335 USPATFULL on STN  
 ACCESSION NUMBER: 80:10301 USPATFULL  
 TITLE: Substrate for the quantitative determination of plasminogen activators  
 INVENTOR(S): Svendsen, Lars G., Reinach, Switzerland  
 PATENT ASSIGNEE(S): Pentapharm A.G., Basel, Switzerland (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4190574		19800226	<--
APPLICATION INFO.:	US 1977-798426		19770519	(5)

	NUMBER	DATE
PRIORITY INFORMATION:	CH 1976-6816	19760528
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Phillips, Delbert R.	
LEGAL REPRESENTATIVE:	Pennie & Edmonds	
NUMBER OF CLAIMS:	5	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	1382	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A substrate for the quantitative determination of enzymes in human and mammal body fluids and tissue extracts, which has the structure

R.sup.1 --X--Y--Z--NH--R.sup.2

wherein X represents a group having the formula ##STR1## in which R.sup.3 is a straight or branched alkyl radical having 1 to 7 carbon atoms or a cyclohexyl or cyclohexylmethyl radical, Y represents a seryl group or a group having the formula --NH--(CH.sub.2).sub.n --CO-- in which n is an integer from 1 to 7, Z represents an arginyl or lysyl group, R.sup.1 represents hydrogen or an acyl or sulfonyl group and R.sup.2 represents an aromatic hydrocarbon radical which optionally may carry substituents.

L6 ANSWER 328 OF 335 USPATFULL on STN  
 ACCESSION NUMBER: 78:21498 USPATFULL  
 TITLE: Process for isolating fibrinolytic substances  
 INVENTOR(S): King, John Burnham, Sandown Lodge, Glebe Rd., Rondebosch, Cape, South Africa

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4086140		19780425	<--
APPLICATION INFO.:	US 1977-801348		19770527	(5)
RELATED APPLN. INFO.:	Division of Ser. No. US 1975-628006, filed on 3 Nov 1975, now patented, Pat. No. US 4039658 which is a division of Ser. No. US 1973-347254, filed on 2 Apr 1973, now abandoned			

	NUMBER	DATE
PRIORITY INFORMATION:	ZA 1972-2311	19720405
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Shapiro, Lionel M.	
LEGAL REPRESENTATIVE:	Behr, Omri M.	
NUMBER OF CLAIMS:	6	

EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 1 Drawing Page(s)  
LINE COUNT: 381

AB A new fibrinolytic enzymatic product having also anticoagulant properties is recovered from bile. It can be further purified to yield several fractions, all having similar activities, their molecular weights varying between about 5,000 and 50,000. The product or its fibrinolytically active derivatives are used to dissolve fibrin and inhibit blood coagulation in vivo or in vitro.

L6 ANSWER 329 OF 335 USPATFULL on STN  
ACCESSION NUMBER: 78:14155 USPATFULL  
TITLE: Preparation of enteric coated digestive enzyme compositions  
INVENTOR(S): Sipos, Tibor, Lebanon, NJ, United States  
PATENT ASSIGNEE(S): Johnson & Johnson, New Brunswick, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4079125		19780314	<--
APPLICATION INFO.:	US 1976-744902		19761126	(5)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1975-585621, filed on 10 Jun 1975, now abandoned			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Rosen, Sam			
NUMBER OF CLAIMS:	30			
EXEMPLARY CLAIM:	1			
LINE COUNT:	1027			

AB Improved enteric coated digestive enzyme-containing compositions which are capable of withstanding hours of exposure to gastric fluids while protecting the biological activity of the enzymes and thereafter releasing the digestive enzymes in their biologically active state within 5 to 30 minutes after being exposed to intestinal fluids, these compositions comprising (a) an enzyme concentrate in (b) a binder system comprising at least about 0.5 wt. %, preferably about 1 to about 10 wt. % (based on the weight of the binder system plus enzymes) of (i) a binder, preferably selected from the group consisting of polyvinylpyrrolidone, microcrystalline cellulose (Avicel), cellulose acetate phthalate, methylcellulose and alginic acid, and preferably (ii) from about 0.1 to about 10 wt. % of a stabilizer, preferably selected from the group consisting of calcium carbonate, polyvinylpyrrolidone, cellulose acetate phthalate, methylcellulose, alginic acid, starch and modified starches, e.g., carboxymethyl starch (Primojel); and (c) from about 0.1% to about 30 wt. %, based on the weight of the total composite (enzyme plus binder system plus disintegrant) of a disintegrant, preferably selected from the group consisting of citric acid, sodium carbonate, sodium bicarbonate, calcium carbonate and other suitable carbonates, alginic acid, starch and modified starches, e.g., carboxymethyl starch (Primojel) are prepared by a process in which the presence of water is avoided and which includes the step of blending enzyme, binder and disintegrant in the presence of a selected inert solvent as well as the subsequent coating of the resulting enzyme/binder/disintegrant composite with from about 2.5% to about 10% by weight, based on the weight of the enzyme/binder/disintegrant composite, of a gastric juice insoluble, intestinal juice soluble, non-porous, pharmaceutically acceptable enteric coating polymer.



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☐ 1: Biochem J. 1995 Apr 15;307 ( Pt 2):471-9.

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## Isolation and characterization of the chicken trypsinogen gene family.

Wang K, Gan L, Lee I, Hood L.

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Department of Molecular Biotechnology GJ-10, University of Washington, Seattle 98195, USA.

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Based on genomic Southern hybridizations and cDNA sequence analyses, the chicken trypsinogen gene family can be divided into two multi-member subfamilies, a six-member trypsinogen I subfamily which encodes the cationic trypsin isoenzymes and a three-member trypsinogen II subfamily which encodes the anionic trypsin isoenzymes. The chicken cDNA and genomic clones containing these two subfamilies were isolated and characterized by DNA sequence analysis. The results indicated that the chicken trypsinogen genes encoded a signal peptide of 15 to 16 amino acid residues, an activation peptide of 9 to 10 residues and a trypsin of 223 amino acid residues. The chicken trypsinogens contain all the common catalytic and structural features for trypsins, including the catalytic triad His, Asp and Ser and the six disulphide bonds. The trypsinogen I and II subfamilies share approximately 70% sequence identity at the nucleotide and amino acid level. The sequence comparison among chicken trypsinogen subfamily members and trypsin sequences from other species suggested that the chicken trypsinogen genes may have evolved in coincidental or concerted fashion.

PMID: 7733885 [PubMed - indexed for MEDLINE]

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☐ 1: U15155. Gallus gallus try...[gi:603902]

Links

LOCUS GGU15155 864 bp mRNA linear VRT 26-OCT-1995  
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 VERSION U15155.1 GI:603902  
 KEYWORDS  
 SOURCE Gallus gallus (chicken)  
 ORGANISM Gallus gallus

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 Archosauria; Aves; Neognathae; Galliformes; Phasianidae;  
 Phasianinae; Gallus.

REFERENCE 1 (bases 1 to 864)  
 AUTHORS Wang, K., Gan, L., Lee, I. and Hood, L.  
 TITLE Isolation and characterization of the chicken trypsinogen gene family

JOURNAL Biochem. J. 307 (Pt 2), 471-479 (1995)

MEDLINE 95251611

PUBMED 7733885

REFERENCE 2 (bases 1 to 864)

AUTHORS Wang, K.

TITLE Direct Submission

JOURNAL Submitted (27-SEP-1994) Kai Wang, Department of Molecular  
 Biotechnology, University of Washington, Seattle, WA 98195, USA

FEATURES Location/Qualifiers

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5'UTR

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sig peptide

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☐ 1: Arch Biochem Biophys. 1970 Feb;136(2):529-40.

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## Human pancreatic proteins: amylase, proelastase, and trypsinogen.

Allan BJ, Zager NI, Keller PJ.

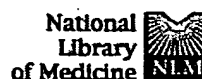
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PMID: 5435442 [PubMed - indexed for MEDLINE]

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☐ 1: FEBS Lett. 1976 Feb 15;62(2):150-3.

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## Activation peptide of human trypsinogen 2.

Guy O, Bartelt DC, Amic J, Colomb E, Figarella C.

PMID: 1253977 [PubMed - indexed for MEDLINE]

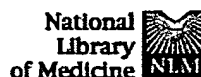
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☐ 1: Biochim Biophys Acta. 1978 Nov 1;543(4):450-4.

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## Demonstration of human pancreatic anionic trypsinogen in normal serum by radioimmunoassay.

Largman C, Brodrick JW, Geokas MC, Johnson JH.

PubMed  
Services

A specific radioimmunoassay for human pancreatic anionic trypsin has been developed. The trypsin employed as radioiodinated tracer in the assay was inactivated with tosyl-L-lysine chloromethyl ketone in order to prevent binding of the tracer to the serum inhibitors alpha1-antitrypsin and alpha2-macroglobulin. A normal serum level of immunoreactive anionic trypsin of 5.45 ng/ml was determined. The results of experiments in which serum was fractionated by Sephadex G-200 gel filtration suggest that essentially all of the immunoreactive material in normal human serum is trypsinogen. This finding implies that a small fraction of the zymogens synthesized in the pancreas are released directly into the circulation.

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☐ 1: Am J Physiol. 1979 Jan;236(1):E77-83.

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## Determination of human pancreatic cationic trypsinogen in serum by radioimmunoassay.

Geokas MC, Largman C, Brodrick JW, Johnson JH.

PubMed  
Services

A specific radioimmunoassay has been developed for human pancreatic cationic trypsin. The assay has been employed for the determination of immunoreactive forms of pancreatic cationic trypsin in blood. The trypsin employed as radioiodinated tracer in the assay was inactivated with tosyl-L-lysine chloromethyl ketone (TLCK) to prevent binding of the tracer to the serum inhibitors while maintaining its immunoreactivity. The average normal serum level determined was 26 ng/ml, with a range of 12--41 ng/ml. Eight of nine patients with acute pancreatic inflammation had at least a 15-fold elevation of total serum immunoreactive cationic trypsin. Cationic trypsinogen and cationic trypsin bound to alpha1-antitrypsin cross-react strongly in the radioimmunoassay. Thus it is possible to measure these potential molecular forms of cationic trypsin in serum. When normal human serum was fractionated on Sephadex G-200, all of the immunoreactive material eluted as a single peak of approximately 23,000 mol wt. No cationic trypsin could be detected in association with alpha1-antitrypsin or alpha2-macroglobulin. The 23,000-mol-wt peak was definitively shown to contain trypsinogen by affinity chromatography and by activation with human enteropeptidase. The identification of cationic trypsinogen in blood implies that the zymogen is secreted into the circulation by the pancreas rather than entering the bloodstream via absorption from the intestine.

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☐ 1: J Biol Chem. 1978 Apr 25;253(8):2732-6.

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### **Human cationic trypsinogen. Purification, characterization, and characteristics of autoactivation.**

**Brodrick JW, Largman C, Johnson JH, Geokas MC.**

PubMed  
Services

Human pancreatic cationic trypsinogen has been purified to homogeneity from an acetone powder of pancreatic tissue. After an initial ion exchange chromatography step on sulfopropyl (SP)-Sephadex at pH 2.6, cationic trypsinogen was separated from the majority of trypsin activity by passage through an affinity column of lima bean trypsin inhibitor-agarose at high ionic strength. The zymogen was then further purified by affinity chromatography on the same material at low ionic strength. Highly purified trypsinogen was resolved from containing chymotrypsinogen by ion exchange chromatography on SP-Sephadex at pH 6.0. The purified zymogen was shown to be homogeneous by polyacrylamide gel electrophoresis at pH 2.1 and at pH 4.3 as well as by discontinuous sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The autoactivation of human trypsinogen was investigated at pH 5.6 and at pH 8.0. The rate of autoactivation of the human zymogen is rapid at pH 5.6 and is maximal in approximately 1 mM  $\text{Ca}^{2+}$ . These results are in marked contrast to those previously reported for autoactivation of bovine trypsinogen, which is extremely slow at pH 5.6 and which shows a dependence on at least 50 mM  $\text{Ca}^{2+}$  for maximum rate of activation (MacDonald, M. R., AND Kunitz, M. (1941) J. Gen. Physiol. 25, 53-73).

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☐ 1: Gene. 1993 Dec 22;136(1-2):167-75.

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## Cloning of the cDNA encoding human brain trypsinogen and characterization of its product.

Wiegand U, Corbach S, Minn A, Kang J, Muller-Hill B.

PubMed  
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Institut fur Genetik, Universitat zu Koln, Germany.

We designed degenerated oligodeoxyribonucleotide primers derived from amino acid (aa) sequences of the highly conserved active sites of mammalian serine proteases (SPs). These primers were used to selectively amplify, in polymerase chain reactions (PCRs), cDNA fragments coding for a SP. We used poly(A)+RNA from human brain to obtain cDNA fragments and amplified one cDNA encoding a novel SP. The full-length nucleotide (nt) sequence was identified by PCR and screening a genomic library in order to obtain the 5'-region. The deduced as sequence shows a high degree of homology to trypsinogens, except for the first exon. In addition to this brain-specific trypsinogen, there exists a variant of the cDNA in pancreas, differing only in the nt sequence of the first exon. An active form of the trypsin was synthesized in vitro and purified by affinity chromatography using soybean trypsin inhibitor (STI) agarose to demonstrate the trypsin-specific interaction with a naturally occurring inhibitor of trypsins.

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